Circulating osteoprotegerin is not removed through haemodialysis membrane

Sir,

We read with interest the study of Coen et al. [1], which suggested a possible relationship between circulating osteoprotegerin (OPG) and bone metabolism in uraemic patients. We also reported that circulating OPG levels were elevated in dialysis patients and that the elevated OPG levels returned to normal after kidney transplantation [2,3]. The data suggested a potential role of the kidney in OPG elimination.

To further elucidate the kinetics of OPG in long-term dialysis patients, we examined whether OPG was removed by haemodialysis. Fifteen adult chronic haemodialysis patients without any residual renal function entered the study. None of them suffered from liver dysfunction. After the circuit was filled with the patients’ blood, samples were obtained from upstream of the high-flux polysulfon membrane haemodialyzer (PS 1.6U, Fresenius-Kawasumi, Tokyo, Japan) at the beginning (P) and the end (R) of the haemodialysis session, and from downstream of the dialyzer at the beginning (Q). The in vitro sieving coefficient of the polysulfon dialysis membrane was 0.79 for beta-2 microglobulin and was less than 0.01 for albumin at the condition of blood flow rate \((QB) = 200 \text{ ml/min}\) and filtrate flow rate \((QF) = 10 \text{ ml/min/m}^2\). In addition to OPG, serum urea nitrogen (UN), beta-2 microglobulin, and albumin levels were simultaneously monitored as controls. Serum OPG concentration was assayed by an ELISA (Cosmo-Bio, Tokyo, Japan).

The serum OPG levels in blood P, Q, and R samples were all comparable with each other, suggesting that OPG molecules were not removed through the polysulfon membrane at all. In contrast, serum UN and beta-2 microglobulin levels decreased in Q and R samples compared with P samples. Serum albumin showed a similar behaviour as that of OPG (Figure 1).

The data indicated that circulating OPG was not removed through polysulfon haemodialysis membrane. The observation is compatible with the supposed size of OPG monomer (approximately 60 kDa) and homodimers in the circulation. Furthermore, such molecules seem unlikely to be eliminated through glomerular filtration in physiological condition.

Fig. 1. The serum OPG levels in the blood samples P, Q, and R were all comparable with each other. The serum urea nitrogen (UN) and beta-2 (β2M) microglobulin levels significantly decreased in the samples obtained from Q and R when compared to that from P. Albumin (Alb) showed a similar trend to OPG.
Thus, the cause of OPG accumulation in uraemic serum remains unknown. We presume that the kidney may play an important role in OPG metabolism. Accumulation of OPG may modify bone metabolism in uraemic patients as a basic mechanism linked to chronic renal failure [4].

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